SUMMARY MINUTES

MEETING OF THE NEUROLOGICAL DEVICES ADVISORY PANEL

OPEN SESSION

February 23, 2004

Gaithersburg Hilton

Gaithersburg, MD

NEUROLOGICAL DEVICES ADVISORY PANEL MEETING

February 23, 2004

Open Session

Attendees

Acting Chair

Kyra J. Becker, M.D.
University of Washington School of Medicine

Voting Members

Fernando G. Diaz, M.D., Ph.D.
Detroit Medical Center

Jonas H. Ellenberg, Ph.D.
Westar

Stephen J. Haines, M.D.
University of Minnesota

Christopher M. Loftus, M.D., F.A.C.S.
University of Oklahoma Health Sciences Center

Deputized Voting Members

Thomas G. Brott, M.D.
Mayo Clinic

Colin P. Derdeyn, M.D.
Washington University School of Medicine

Annapurni Jayam-Trouth, M.D.
Howard University College of Medicine

Mary E. Jensen, M.D.
University of Virginia Health Sciences Center

Andrew Ku, M.D.
Allegheny Radiology Associates

John R. Marler, M.D.
National Institute of Neurological Disorders and Stroke

Consumer Representative

Crissy E. Wells, R.T., M.B.A., M.H.S.A.
Western Regional Community Clinical
Oncology Program

Industry Representative

Andrew K. Balo
DexCom, Inc.

Food and Drug Administration Participants

Janet L. Scudiero, M.S.
Panel Executive Secretary

Celia Witten, M.D., Ph.D.
Director, Division of General, Restorative,
and Neurological Devices

Neil Ogden
Chief, General Surgery Devices Branch

Michael J. Schlosser, M.D.
Medical Officer
General Surgery Devices Branch

Judy S. Chen, M.S.
Mathematical Statistician
Office of Surveillance and Biometrics

CALL TO ORDER

Panel Executive Secretary Janet L. Scudiero, M.S., called the meeting to order at 9:33 a.m. She noted that the tentatively scheduled April 1 and 2 Neurological Devices Panel meeting had been cancelled. The remaining tentatively scheduled meetings for 2004 are August 5 and 6 and October 28 and 29.

Ms. Scudiero read the conflict of interest statement, which stated that the Agency had taken into consideration certain matters regarding Drs. Thomas G. Brott, Colin P. Derdeyn and John R. Marler, who reported past or current interests involving firms at issue; the Agency had determined that they may participate fully. Ms. Scudiero noted that Dr. Kyra J. Becker is the acting panel chair for the duration of the meeting. The following participants had been granted temporary voting status for the duration of the meeting: Drs. Thomas G. Brott, Colin P. Derdeyn, Annapurni Jayam-Trouth, Mary E. Jensen, Andrew Ku, and John R. Marler.

Panel Chair Becker stated that the purpose of the meeting was to make a recommendation to the FDA on the clearance of a 510(k) submission for the Concentric Medical, Inc., Mechanical Embolus Retrieval in Cerebral Ischemia (MERCI) Retriever. Dr. Becker asked the panel members to introduce themselves and noted for the record that the voting members present constituted a quorum.

FDA UPDATE

Neil R. Ogden, Chief, General Surgery Devices Branch, stated that a final rule to classify human dura mater into Class II was finalized in January 2004. A special controls draft guidance for vascular and neurovascular embolization devices will be published in February 2004.

SPONSOR PRESENTATION

Mr. Kevin MacDonald, Vice President of Clinical and Regulatory Affairs, Concentric Medical, introduced Concentric's presenters, gave an overview of the company's presentation, described the company, and summarized the MERCI Retriever's regulatory history. The device is identical to Concentric's Foreign Body Retriever, which has already been approved for removal of foreign bodies in the neuro, coronary, and peripheral vasculatures. The MERCI

Retriever is intended to restore blood flow in the neurovasculature by removing thrombus in patients experiencing an ischemic stroke.

Gary Duckwiler, M.D., Professor of Radiology and Neurosurgery, UCLA Medical Center, presented data on stroke incidence. Of the 700,000 strokes each year in the United States, 85 percent are ischemic, and 70 percent are large-vessel occlusions. Current stroke treatment options are limited—only intravenous tissue plasminogen activator (tPA) is FDA approved. Physicians use a variety of off-label treatments for patients suffering from stroke, including mechanical means for dealing with clots, such as baskets, snares, balloons, and aspiration devices.

The MERCI Retriever is a flexible, tapered Nitinol wire with a helical tip that comes in three sizes. It is used in conjunction with a balloon guide catheter, and a microcatheter. One of the safety features of the MERCI Retriever is that if it encounters resistance, the coil straightens out.

Wade Smith, M.D., Ph.D., Director, Neurovascular Service, UCSF, explained the NIH Stroke Scale (NIHSS) score and the modified Rankin Scale (mRS), which were used in the MERCI study. In the trial, neurovascularization was defined as restoration of blood flow to all treatable vessels. The trial used thrombolysis in myocardial infarction (TIMI) flow to measure revascularization.

The MERCI trial is a prospective, single-arm, multicenter, nonrandomized study. Safety was overseen by a data safety monitoring board (DSMB). The study hypothesis was that the retriever could access and revascularize occluded vessels in patients experiencing ischemic stroke while minimizing adverse events. The primary endpoints were successful revascularization in all treatable vessels and while limiting serious adverse events (SAEs). Secondary endpoints were patients' neurological status at 30 and 90 days using NIHSS score and mRS. Study success was defined as successful revascularization of at least 30 percent of patients and statistical superiority to the 18 percent benchmark derived from the Prolyse in Acute Cerebral Thromboembolism (PROACT) II study control.

Dr. Smith listed the study inclusion and exclusion criteria. Patients had to fall into one of two groups: those who had been experiencing stroke symptoms for up to 3 hours and were contraindicated for tPA or those who had been experiencing symptoms for 3 to 8 hours, and with an angiogram demonstrating a thrombotic occlusion in the internal carotid artery, M1, or M2

segment of the middle cerebral artery (MCA), basilar artery, or vertebral artery. Phase 1 of the study excluded patients with occlusions in the M2 segment. Twenty-five sites participated. Of the 121 enrolled patients (intent to treat), 114 patients were treated at the time of the sponsor's submission. Forty-six percent of participants were women; the median participant age was 71; median baseline NIHSS score was 19 and median time from symptom onset to final angiogram was 6.1 hours.

Gene Sung, M.D., M.P.H., Director, Neurocritical Care and Stroke Program, University of Southern California, presented information on the composition and role of the DSMB. Stopping rules were established for hemorrhage rates and mortality. SAEs were defined as vessel perforation, intramural arterial dissection, and significant embolization in a previously uninvolved arterial territory. SAEs through 90-day follow-up were defined as death, new stroke, and myocardial infarction. Four of 114 patients (3.5%) experienced serious device-related adverse events: Two patients experienced stroke in previously uninvolved territory, and two experienced dissection or vessel perforation. SAEs consisted of 45 deaths, two new strokes, and two myocardial infarctions. Symptomatic or device-related hemorrhage occurred in nine patients (7.9%); four were disease related, three were stroke-related, and two were device related. Asymptomatic hemorrhage occurred in 33 patients (28.9%).

A total of 265 devices were used in 114 patients; seven devices fractured; of those, six device tips detached in patients, two of which were retrieved. In only one case was there negative clinical sequelae as a result of the tip fracture; however, four deaths occurred in the group of patients in whom devices fractured. Device mechanical failures were thoroughly evaluated, and corrective actions were implemented. All safety criteria were met in accordance with the DSMB stopping rules.

Dr. Smith presented the safety and effectiveness results. He stated that the issue for clearance of the 510(k) is the rate of device-related events, not all procedure-related events. He noted that the FDA analysis found a higher number of SAEs, but the Agency included symptomatic intracranial hemorrhage (ICH), which the sponsor did not view as a device-related SAE. The FDA analysis also found three instances of arterial dissection (the sponsor considered these procedure, and not device-related.) One arterial perforation occurred following tip detachment and subsequent retrieval efforts. The FDA analysis determined that a fourteen patients experienced SAEs and eight patients experienced device- or procedure-related SAEs; the

sponsor's analysis found that four patients experienced device-related SAEs and four patients experienced procedure-related SAEs.

The study achieved a 53.5 percent revascularization rate (50.4% in the intent-to-treat population), defined as TIMI II or III flow achieved in the target vessel(s) with the MERCI Retriever alone. That rate was statistically superior to the benchmark in both groups.

NIHSS score and mRS in revascularized patients were significantly better than in nonrevascularized patients. Death, new stroke, and myocardial infarction occurred more frequently in non revascularized patients. The sponsor also analyzed the data by the occlusion location and vessels treated. In all cases, revascularized patients had better mRS scores. In addition, MERCI patients experienced equivalent mortality to comparable groups in the published literature.

The sponsor compared MERCI data with data from the control group in the PROACT II trial. MERCI patients experienced numerically higher (but not statistically different) mortality and had a wider range and higher median pre-procedure NIHSS score than the PROACT II group. The symptomatic hemorrhage rate was numerically, (but not statistically higher) in the MERCI group.

The sponsor conducted univariate analysis to attempt to find correlations between numerous baseline characteristics and the outcome of mRS = 2 at 30 days after treatment. Only three variables were found to have any correlation to this outcome. Successful revascularization was positively correlated with mRS = 2, whereas baseline NIHSS score and number of attempts to remove clot were negatively correlated with mRS = 2. Age and other risk factors were not related to outcomes. Age was a predictor of being able to open a vessel—the older the patient was, the more likely was the patient to be successfully revascularized.

The sponsor concluded by stating that the primary study endpoint was achieved because successful revascularization in all treatable vessels was achieved in 53.5 percent of patients; the target was 30 percent. In addition, treatment with the device showed promising results regarding neurological outcomes. The sponsor concluded that they had met the endpoints for clearance of the device.

Panel Questions for the Sponsor

Panel members asked for more information on whether the device could be used with angioplasty for a fixed lesion; how the MERCI participants' angiograms were graded; characteristics of the patients who were ineligible for tPA and reasons for their ineligibility, whether the MERCI patient population was representative, time between eligibility angiogram and time of treatment; why physicians were overtorquing the device, causing device fracture; definition of adverse events; total procedural complication rate; reasons for the rates of ICH in the MERCI study; heparin dose given to patients and the drug's relation to ICH; correlations between adverse event and mortality rates and treatment site; whether the study was powered adequately; patient exposure to ultrasound; complication rates for the predicate device when used to retrieve foreign bodies; and the criteria on which a physician might base a decision to use the MERCI Retriever over another treatment approach. Sponsor representatives answered the panel's questions.

FDA PRESENTATION

Michael J. Schlosser, M.D., Medical Officer, General Surgery Devices Branch, reviewed the device description. He stated that it is a legally-marketed device. The device used in the study is nearly identical to the device that was approved in the initial 510(k) and therefore, the biocompatibility; performance, testing, and other bench testing were submitted and reviewed as adequate by FDA. The sponsor has made minor modifications to address tip fracture; the sponsor has submitted bench testing of those modifications to the Agency.

He stated that the objective of the MERCI study was to demonstrate safe revascularization, not improved clinical outcome. Dr. Schlosser reviewed the clinical protocol and noted that the sponsor had adequately described the device's operation.

FDA's safety analysis defined vessel perforation, vessel dissection, symptomatic ICH, and embolization into a previously uninvolved territory as the most important outcomes. All adverse events were reported on case report forms and submitted to FDA. The investigators and the DSMB analyzed each SAE to determine whether it was device related or procedure related. FDA found a total SAE rate of 12 percent. The device- and procedure-related SAE rate was 7 percent (8 of 114 patients). Because asymptomatic ICH is common in stroke populations, the Agency focused on symptomatic ICH. Compared with placebo patients in the PROACT II trial,

MERCI patients had numerically higher mortality and symptomatic ICH rates but lower groin hematoma rates.

Dr. Schlosser also reviewed an updated efficacy outcome data set (n = 129); the results were comparable to those found for the original 114 patients. All results met the primary endpoint success criteria of achieving at least a 30% revascularization rate.

Dr. Schlosser stated that the MERCI trial did not use a control group. It was not powered to demonstrate clinical benefit of treatment in patients suffering from acute stroke, only to demonstrate successful restoration of blood flow. However, the mRS and NIHSS scores at 30 and 90 days for patients in the MERCI trial were compared with the results published on the placebo group of the PROACT II study to ensure that outcomes in the MERCI trial were no worse than those reported for the PROACT II study. The two study populations had several important differences: 1) NIHSS score inclusion criteria were 4 to 30 for PROACT II and >8 for MERCI; 2) MERCI included internal carotid artery, MCA, and posterior circulation lesions, whereas PROACT II included only MCA lesions; 3) MERCI excluded patients who were candidates for tPA; and 4) PROACT II used stricter exclusion criteria with reference to risk factors for hemorrhage. Although some clinical outcomes were slightly worse for the MERCI patients, Dr. Schlosser pointed out that the outcomes are statistically no different and have to be evaluated in light of the general weakness of the comparison. The sponsor succeeded in its "no worse than" analysis. A comparison across the two studies of clinical outcomes for patients with MCA occlusions found a slightly better outcome among MERCI patients, but the comparison is flawed for the four reasons stated above.

In an additional post hoc analysis, the clinical outcomes were compared for patients in whom revascularization with the MERCI Retriever succeeded at restoring TIMI grade II or III flow to those in whom flow was not restored with the MERCI Retriever alone. Patients who were revascularized with an additional therapy after failure of the MERCI Retriever were considered unsuccessful for these analyses. Patients who were successfully revascularized had a lower mortality, and did better clinically, as demonstrated by mRS scores at 90 days; however, the data permit no firm conclusions.

In summary, the device has a 48 percent adverse event–free revascularization rate, a 12 percent SAE rate, a 6 percent device- or procedure-related SAE rate, and a rate of symptomatic ICH of 8 percent. A trend toward improved outcome in the subset of MCA patients was seen

when compared with PROACT II patients. The decrease in mortality and increase in the rate of good outcome when comparing patients with successful revascularization to those with unsuccessful treatment may indicate that revascularization is beneficial.

Judy S. Chen, M.S., Mathematical Statistician, Office of Surveillance and Biometrics, provided FDA's statistical review. She reiterated that revascularization, not clinical outcome, was the primary effectiveness endpoint. Due to the differences in inclusion criteria, baseline NIHSS score was higher among MERCI Retriever patients than among PROACT II patients. The MERCI and PROACT II patients are not especially comparable, so the PROACT II study is not a good control. The mortality data for the MERCI patients are worrisome; the differences between the MERCI patients and the PROACT II patients are not statistically significant, but the groups are not statistically equivalent, so one cannot place great weight on the comparison. MERCI patients who were successfully revascularized had improved mortality rates over the patients who were not successfully revascularized. Data from the MERCI study showed that baseline variables such as age, mRS, and systolic blood pressure also significantly affected mortality. No statistically significant prognostic factor for successful revascularization was found, however. Thus, although 48 percent of patients treated with the MERCI Retriever had successful revascularization, the effects on clinical outcomes are unclear.

Panel Questions for FDA

Several panel members' questions focused on the rationale for FDA's decision to forgo a trial that examined clinical outcomes; Dr. Witten clarified the Agency's approach to determining substantial equivalence and noted that the device is already on the market as a foreign body retriever. Panel members also expressed concern over the definition of adverse events used in the study, ICH rates, the lack of a suitable control group, lack of data on outcomes for patients who did not receive treatment, and the relatively high mortality rates in the MERCI study.

OPEN PUBLIC HEARING

Adnan I. Qureshi, M.D., Professor and Director, Cerebrovascular Program, University of Medicine and Dentistry of New Jersey, presented information on methodological considerations for Phase I and II trials for new devices for ischemic stroke. He

presented suggestions for defining study populations, interventions, measures of feasibility, and measures of safety, and he presented a stroke-grading scheme that takes into account severity and collaterals and helps predict outcomes. Standardization of Phase I and II trials for evaluating devices for treatment of ischemic stroke will help address whether a device has the potential to develop into meaningful treatment, ensure that safety endpoints are below the thresholds established by previous clinical studies, and ensure comparability between trials and endpoints.

Afshin A. Divani, Ph.D., Head, Cerebrovascular Research Group, Cerebrovascular Program, University of Medicine and Dentistry of New Jersey, discussed methodological issues related to preclinical studies for evaluating thrombectomy devices. He reviewed the pros and cons of primate, canine, and swine animal models with regard to accessibility to the vascular system, vascular architecture, and thrombus injection. The simplest and most cost-effective model should be chosen for proof of concept and mechanical performance in the first round of device evaluation. In subsequent testing, a more sophisticated model should be used to evaluate how thrombectomy devices improve outcomes for patients experiencing cerebral ischemia.

PANEL REVIEWS

Dr. Jensen noted that the MERCI Retriever is currently approved as a foreign body retrieval device. Her analysis took into account the fact that thrombus retrieval using this device requires the use of multiple components that cannot be considered in isolation from each other.

A primary concern is the device fracture rate. Preclinical torque testing found an average of 33 rotations to failure, but the device is not intended to be rotated that much during use. Almost 10 percent of devices had some type of failure, which appear to be linked to overtorquing. The sponsor has modified the device and revised the instructions for use to address the concern. Nevertheless, questions remain: Was bench testing a true measure of the device's tolerances? Is clot type important in device failure? What role does vasospasm play in tip trapping? Should testing be required in animal models for clot retrieval devices? Are there unknown materials issues? Why are so many operators overtorquing the device? Is performance not what was expected, or is training required?

Reviewing the clinical study, Dr. Jensen noted that the sponsor's materials indicated that the study would compare the MERCI Retriever to "other catheter-based interventions including foreign body retrieval with the predicate device, the Concentric Retriever." However, the

findings do not mention the percentage of serious device-related events occurring with use of the predicate device or other such devices. The omission raises questions: How many devices have been sold? In which vascular territories have they been used? How many device failures or complications have occurred with the predicate device? The study does not mention long-term follow-up considerations for patients with retained fragments.

A total of thirteen procedure-related adverse events occurred, eleven of which were considered severe or life-threatening. The safety findings raise several questions: What role does thrombolysis play in ICH? What is the complication rate of the predicate device when used intracranially? Should the balloon catheter be considered part of the device? Two serious complications occurred due to the balloon catheter; how many of the complications were due to the need for a larger guiding catheter or sheath than routinely is used? What were the complication rates in the PROACT II trial for groin complications and parent artery dissection? Did posttreatment angiograms demonstrate important findings outside of the adverse events, such as the presence of vasospasm or distal emboli in targeted territory? Is the device oversized for M2 branches? Finally, how should the patients with retained fragments be followed?

The study's strengths are that it was prepared in conjunction with FDA, was prospective, compared data from a trial with same target disease and site, was conducted at experienced centers, and included neurological outcomes as secondary endpoints. Study weaknesses are that it was not randomized, used a patient population not wholly similar to the PROACT II population, used numerous sites with differential enrollment, and permitted mixing of treatments (i.e., some patients had thrombolysis following clot retrieval). The methodology leads to speculation about outcomes. The sponsor had incomplete data collection on neurologic examinations, lacked long-term safety data, and provided incomplete explanation for technical issues.

Dr. Jensen raised several training issues. How should users be trained on the device, and who can use it? Should training be mandatory, involve proctoring, or both? Finally, she noted that if the device was cleared, physicians might feel pressure to choose the device over intraarterial thrombolysis and patient expectations might increase. The device is already being touted in the lay press as the newest stroke therapy.

Dr. Brott raised several safety concerns. He noted that the sponsors did not have access to the PROACT II database, but data from the tPA trial is publicly available. How does MERCI

compare with patients who received no treatment in the tPA study? Publicly available tPA data are more comparable than the PROACT II data, because tPA patients represented the gamut of anatomy. A data set that matches patients on NIHSS score and other covariates is needed.

Sponsor representatives responded to Dr. Jensen's and Brott's concerns.

Dr. Ellenberg focused on methodological and statistical issues. He noted that the MERCI trial participants were not eligible for thrombolytics and may have been at higher risk for a poor outcome. The PROACT II control may not have been appropriate, particularly because the studies were nonconcurrent. The MERCI trial involved multiple vasculature types. Although some available data (e.g., age, smoking, and baseline NIHSS score) were used to predict success, other important and unavailable data were not collected, such as clot density, size, location, and procedure length. Success cannot be predicted with the available covariates. The results leave little guidance for patient selection. The PROACT II study participants were drawn from a much larger population than the MERCI trial participants; more information is needed about the population that the MERCI trial participants reflect. The PROACT II group was not an appropriate comparator for the MERCI group.

The univariate analysis found that revascularization success predicted mortality, but the multivariate analysis did not show that revascularization predicts mortality after accounting for baseline NIHSS score and systolic blood pressure. Further multivariate analysis of the risk of mortality for revascularized and nonrevascularized patients is needed. Problems with the multivariate logistic model approach include inconsistencies between the univariate and multivariate analyses, deletion of collinear covariates, and rerunning the analysis for MCA only. Nothing is known about what characteristics—NIHSS score, blood pressure, or age—might have led to success or nonsuccess. Ultimately, the clinical outcome is what is important.

PANEL DELIBERATIONS

Panel members reiterated many of their concerns. They noted the fracture problems resulting from torque, the lack of data on clinical outcomes, the problems with the statistical analysis and study methodology, and the apparent excess mortality in patients who were not successfully revascularized. Many panel members believed that the sponsor did not demonstrate device safety. Some panel members were satisfied that the sponsor had met the Agency's requirements.

FDA Questions for Panel

Question 1: The results of the MERCI trial reported the rates of serious adverse events in the treated population. These were defined in the IDE as: symptomatic intracranial hemorrhage, vessel dissection or perforation, and embolization of clot into a previously uninvolved territory. The rates of these serious adverse events were compared to the rates seen in the placebo group in the PROACT II study, where appropriate.

a. The overall rate of serious adverse events was 13% with serious device- or procedure-related adverse events at 7%. Does this data support the safe use of the device in the removal of clots from the neurovasculature?

b. The overall rate of symptomatic intracranial hemorrhage at 24 hours in the MERCI trial was 8%, higher than the 2% rate seen in the placebo group in the PROACT II trial. Please discuss whether this raises safety concern regarding the use of this device in the proposed patient population.

c. The mortality rate in the MERCI trial was 38%, with a 32% rate seen in patients with MCA occlusions. This shows a trend toward a higher rate than that seen in placebo group in the PROACT II trial (27%). Please discuss whether this raises a safety concern regarding the use of this device in the proposed patient population.

The panel generally concurred that it did not have enough information to determine whether the MERCI trial data demonstrate safety of the device. Excess mortality may result for patients who are not successfully treated. The absence of a control group makes it impossible to make a judgment. Device fractures are a concern. One panel member did not see a safety concern for the proposed treatment population as long as the instructions are modified to try to reduce the rate of device fractures due to excess torquing.

Question 2. The efficacy endpoint in this trial was successful revascularization, defined as achieving TIMI II or III flow. The trial results demonstrate a 52% revascularization rate (intent-to-treat) and a 47% serious adverse event-free revascularization rate. This was statistically significant compared to the spontaneous revascularization rate of 18% seen in placebo group in PROACT II and the goal of > 30% set forth in the IDE. Is this adequate to demonstrate efficacy of the device in restoring flow in occluded vessels within the neurovasculature?

Most panel members concurred that the study demonstrated efficacy for clot removal and revascularization. However, several panel members expressed concern that the term "efficacy" carries clinical implications, and they took pains to clarify that the device's efficacy is limited

only to mechanical clot removal and revascularization. Several panel members expressed concern that the study relied on a comparator group that was not statistically valid.

Question 3. The MERCI trial was designed using successful revascularization as a surrogate endpoint for improved clinical outcomes. Although not the primary endpoint, the sponsor collected 30 and 90 day clinical outcomes (NIHSS and modified Rankin Score) for patients enrolled in the study. Please comment on whether you believe that the results observed, i.e., the trend toward improved clinical outcome in patients where revascularization was successful, supports this surrogate outcome measure.

The panel concurred that the data did not demonstrate revascularization to be a surrogate endpoint. The panel was uneasy that the company was not asked to evaluate clinical outcome. Some panel members were uneasy with the idea of approving a device for treatment of stroke on the basis of a narrow technical criterion. Several panel members suggested that successful revascularization is an appropriate clinical outcome. However, one panel member pointed out that the relevance of this endpoint depends upon the timing, and based upon the MERCI trail, there is not enough evidence to say that at six hours at the time of the last angiogram, revascularization is an appropriate surrogate outcome.

Question 4. One aspect of the Agency's review of a new product is to assess the adequacy of the product's labeling. The labeling must give appropriate instructions for use to the treating physician.

a. Given the results of the MERCI trial, does the indication for use adequately define the patient population that should be treated with the Concentric Retriever? Specifically, should the population be limited in terms of: the time between onset of symptoms to initiation of treatment; location of occlusions that can be treated; the severity of strokes at baseline; or treatment with the Retriever only when a patient is not a candidate for other approved treatment (IV tPA)?

b. Are there any additional warnings or contraindications that should be added to the labeling specifically with reference to adverse events seen in the MERCI trial?

The panel agreed that the data are not sufficient to make labeling recommendations. One panel member suggested that the labeling should make it clear that the device is for removal of an embolic clot from a distant source, not for treatment of stroke. Another panel member said that the labeling should include warnings about excess torque and possible fracture or detachment of the device tip.

PANEL SUMMARY COMMENTS

The panel did not vote on a recommendation, but members were asked to summarize their views. Several panel members stated that such a device would be useful in the armamentarium of options for treatment of patients with stroke and that they would like to use it off-label, but more data are needed to demonstrate its safety and efficacy. A randomized, controlled trial is needed to demonstrate benefit.

ADJOURNMENT

Dr. Witten thanked the participants on behalf of the Agency, and Dr. Becker adjourned the meeting at 3:53 p.m.

I certify that I attended this meeting of the Neurological Devices Advisory Panel Meeting on February 23, 2004, and that these minutes accurately reflect what transpired.

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Janet L. Scudiero, M.S.
Executive Secretary

I approve the minutes of this meeting as recorded in this summary.

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Kyra J. Becker, M.D.
Chairperson